Melanoma of the Skin

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Melanoma is a cancer of the cells that produce and transport the pigment melanin. In the United States, approximately 32,000 new cases of skin melanoma were projected for 1994 (Boring et al., 1994). Melanomas can occur on any skin surface, but in light-skinned populations, a clear excess occurs on the trunk in men, the lower extremities in women, and the head and neck regions and arms in both sexes. In dark-skinned populations, melanomas occur most often on the palms of the hands and the soles of the feet.

The highest melanoma rates occur among light-skinned populations in areas of intense sunlight, e.g., Arizona and Queensland, Australia (World Health Organization et al., 1990). In the United States, data for whites from the NCI Surveillance, Epidemiology, and End Results (SEER) Program show an incidence rate of 12.4 and a mortality rate of 2.5 per 100,000 (Ries et al., 1994). Mortality rates within the United States vary inversely with latitude (Pickle et al., 1987).

Over the last several decades, the incidence of melanoma has increased dramatically in the United States and several other countries, posing a major threat to public health (Devesa et al., 1987; Glass and Hoover, 1989; Ries et al., 1994). In the United States, the reported incidence for whites rose 102 percent from 1973 to 1991. The increase for white males was 124 percent. This rate of increase leads all other cancers, including lung cancer in females. The increase has been most marked in older white males and females. The exact pattern of increase is not certain, because of underreporting, as suggested by higher rates measured in an HMO than in the general population (Glass and Hoover, 1989). For the period 1987 to 1991, the rate of increase, in whites, measured in SEER population registries slowed to 1.8 percent per year (Ries et al, 1994). Nevertheless, there is growing concern that the depletion of the earth's ozone layer and the subsequent increase in the amount of ultraviolet radiation (UVR) reaching the earth may exacerbate the increase in melanoma incidence in the next several decades (Longstreth, 1987).

Melanoma represents only about 5 percent of all skin cancers in the United States, but it accounts for about 75 percent of all skin cancer deaths, about 6,900 deaths per year (Boring et al., 1994). Survival rates have been increasing because more melanomas are being diagnosed at an early stage. For white patients diagnosed between 1983 to 1990, the overall relative 5-year survival rate was 85 percent. Despite a better survival percentage, the total mortality rate continues to increase because of the dramatic increase in incidence.

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Although the precise cause of melanoma is unknown, numerous clinical and epidemiologic studies in the past decade have identified characteristics associated with increased risk of melanoma: a history of sunburns, fair skin, number of moles, presence of dysplastic or other atypical moles, previous melanoma, family history of melanoma, and immunosuppression. Several recent review articles discuss them in greater detail (Rhodes et al., 1987; Evans et al., 1988; MacKie et al., 1989; Koh, 1991; Fraser et al., 1991; and Elwood, 1993).

Sunlight Exposure

Melanoma is related to excessive exposure to ultraviolet radiation (UVR), but not so directly as are the more common nonmelanoma skin cancers, basal cell carcinoma, and squamous cell carcinoma. Most nonmelanoma skin cancers are related to chronic overexposure to UVR, while melanoma appears to be related to intense intermittent exposure to UVR, especially in early life. Several recent studies have found significantly increased risks of melanoma following repeated severe (blistering) sunburns, particularly during childhood and teenage years. Inconsistent associations have been reported with regard to the influence of constant long-term exposure to sun.

Fair Skin

People with fair skin and light eyes and hair experience sun sensitivity because they have less melanin, which protects their skin from the cumulative damage produced by UVR. The fact that these people suntan minimally, or not at all, and sunburn easily presumably explains the high risk among lightly pigmented individuals. Freckles, an indicator of sun sensitivity and sun damage, are associated with increased risk.

Mole Characteristics

Mole patterns, including type and number of moles, are an important risk factor. Most moles (nevi), which are clusters of melanocytes, are benign lesions called common acquired nevi. Rarely, a mole may undergo abnormal changes, and if it is not removed, become a melanoma. Alternatively, some melanomas arise in a skin site where there was not a preexisting mole. A persistently changed or changing mole, particularly in an adult, may be the most important risk factor for the development of melanoma (Rhodes et al., 1987).

Dysplastic nevi identify individuals at increased risk of melanoma, both in the familial and nonfamilial setting. Dysplastic nevi are different from common acquired moles in that they are often larger than normal moles (>6mm, the size of a pencil eraser), have irregular and indistinct borders, have a flat component, and often contain shades of pink, red, and brown. The risk of melanoma is highest for members of melanoma-prone families who have dysplastic nevi and who have already had a melanoma; they are at exceedingly high risk of developing additional primary melanomas (Tucker, 1988). Members of melanoma-prone families with dysplastic nevi but no personal history of melanoma are also at greatly increased risk of melanoma. The risk of melanoma among persons with dysplastic nevi but no family history of either melanoma or dysplastic nevi is increased, but is not nearly so high as in those with a family history of melanoma.

Giant congenital nevi, which are present at birth or develop within the first year of life, are a risk factor for melanoma (Rhodes et al., 1987). The risk of melanoma associated with small congenital nevi is more controversial.

Other Risk Factors

Individuals who have already had one melanoma also have increased risk of developing additional primary melanomas (Rhodes et al., 1987; Evans et al., 1988; Tucker, 1988; MacKie et al., 1989; Koh, 1991; Fraser et al., 1991). People with a family history of melanoma, even without dysplastic nevi, have increased risk. Certain states of immunosuppression are associated with increased risk, e.g., renal transplant recipients and Hodgkin's disease. Individuals with xeroderma pigmentosum, a rare hereditary skin disease, lack an enzyme that normally repairs cellular DNA damaged by UVR and face increased risk of both melanoma and nonmelanoma skin cancers. In addition, significantly elevated risks of melanoma are seen after brain and breast cancer (Tucker, 1988). The increase of melanoma after breast cancer may relate to shared hormonal or reproductive risk factors.

Oral contraceptives were once proposed as a risk factor, but numerous subsequent studies have found no association. Other factors that have been studied and generally found unrelated to risk include: alcohol, caffeine, tobacco, hair dyes, pesticides, marital status, and parity. Fluorescent lighting has been proposed as a risk factor, but has not been extensively studied. Dietary constituents may play a role, but no consistent associations have emerged to date. Similarly, no occupational hazards, apart from UVR exposures, have been identified.

REFERENCES

Boring CC, Squires TS and Tong T: Cancer Statistics 1994. *CA Cancer J Clin* 44:7-26, 1994.

Devesa S, Silverman DT, Young JL Jr, et al.: Cancer incidence and mortality trends among whites in the United States, 1947-1984. *J Natl Cancer Inst* 79:701-770, 1987.

Elwood JM: Recent developments in melanoma epidemiology, 1993. *Melanoma Research* 3:149-156, 1993.

Evans RD, Kopf AW, Lew RL, et al.: Risk factors for the development of malignant melanoma—I: Review of case-control studies. *J Dermatol Surg Oncol* 14:393-408, 1988.

Fraser MC, Hartge P and Tucker MA: Melanoma and non-melanoma skin cancer: Epidemiology and risk factors. *Semin Oncol Nurs* 7:2-12, 1991.

Glass AG and Hoover RN: The emerging epidemic of melanoma and squamous cell skin cancer. *JAMA* 262:2097-2100, 1989.

Koh HK: Cutaneous melanoma (medical progress). *N Engl J Med* 325:171-182, 1991.

Longstreth JD, ed.: Ultraviolet radiation and melanoma with a special focus on assessing the risks of stratospheric ozone depletion. Vol 4 of Assessing the Risks of Trace Gases that can Modify the Stratosphere. Washington, DC: Environmental Protection Agency, 1987.

MacKie RM, Freudenberger T and Aitchison TC: Personal risk-factor chart for cutaneous melanoma. *Lancet* 2:487-490, 1989.

Rhodes AR, Weinstock MA, Fitzpatrick TB, et al.: Risk factors for cutaneous melanoma. A practical method for recognizing predisposed individuals. *JAMA* 258:3146-3154, 1987.

Ries LAG, Miller BA, Hankey BF, et al: SEER Cancer Statistics Review, 1973-1991: Tables and Graphs, National Cancer Institute. NIH Publ. No. 94-2789, Bethesda, MD, 1994.

Tucker MA: Individuals at high risk of melanoma. In Pigment Cell, vol 9 (Makie RM, ed.). Basel, Switzerland: S. Karger, 1988, 95-109.

Whelan SL, Parkin DM and Masuyer E (eds.): Patterns of Cancer in Five Continents. p. 29. World Health Organization, International Agency for Research on Cancer, and International Association of Cancer Registries. IARC Scientific Publication No. 102, Lyon, 1990.